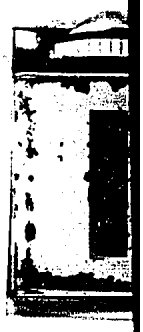
STAT

Sanitized Copy Approved for Release 2011/07/12 : CIA-RDP80-00809A000700240023-8



RECENT USSR WORK ON TRANSPLANTATION OF ORGANS

Meditsinskiy Rabotnik, Vol 18, No 40
Moscow, 13 May 1955

Prof N. Sinitsyn
Gor'kiy

[Comment: This report gives information from an article published under the title "The Problem of the Transplantation of Organs." In addition to the general medical and biological significance of the results reported in the article, the emphasis on pharmacological and toxicological applications is of interest.]

The staff of our laboratory has worked for more than 20 years on the problem of the transplantation of the heart of vertebrate animals. We can successfully carry out this operation on cold-blooded animals, e.g., frogs. The results which have been achieved are of general biological significance and furthermore contribute to the solution of the problem as far as warm-blooded animals are concerned.

In the work on the transplantation of the hearts of frogs, we had to surmount great difficulties connected not only with the operational technique, but also with conditions which prevent the assimilation of the heart in a foreign organism.

The thoroughgoing biological affinity between the tissues of a single organism affects every living cell within this organism. Any organ or tissue which has been artificially separated from the intact organism requires an adequate substrate which will enable it to survive under new living conditions. All deviations from the proper conditions in this substrate disturb the nutrition of the transplanted organ, with the result that the organ perishes.

To transplant successfully a heart or any other organ, a preliminary attenuation of the biochemical specificity of the proteins of the organ being transplanted is essential. This specificity is a distinguishing mark of the organism from which the transplanted organ is derived.

Consequently, one must find methods of transferring the organs to a simpler nutritional regime appropriate to animal organisms of the class in question. In order to achieve this purpose, we kept the heart in an artificial nutrient medium at a low temperature (4 - 6°) for a period of 5 days. By doing this, we achieved a considerable weakening of the individual specificity of the proteins typical for the organism in question. As a result, the rate of survival of frogs to which a heart had been transplanted increased from 10-15% to 70%.

Another important factor on which a successful solution of the problem depends is the reactivity of the body itself. Physiology teaches us that the reactivity of the organism to foreign proteins depends on the initial state of the central nervous system. We assumed that methods by means of which the reactivity of the central nervous system to foreign proteins is inhibited will contribute to the assimilation of an organ that has been transplanted, including the heart.

In order to inhibit the central nervous system, we used sleep therapy. Six to 8 hours prior to the operation, the animal received a large dose of a hypnotic. The operation was then carried out against the background of drug-induced sleep. After the operation, the frog continued to sleep for 24-48 hours. Combining artificially induced sleep with a preliminary storage of the heart to be transplanted at a low temperature and in an artificial nutrient medium for a period of 5 days yielded very good results: the assimilation of transplanted hearts in frogs increased to 85%.

The frogs which survived after the hearts had been transplanted were subjected to a thorough study for a year. Beginning with the first minutes of the work of the heart in the foreign organism, the frequency of heart beats has been determined daily. Furthermore, electrocardiograms are being taken and the blood pressure is being measured.

Every 30 days the transplanted heart of one of the frogs is subjected to microscopic examination. We established that after 45 days the blood vessels of the transplanted heart anastomatize completely with those of the host organism.

Within 90 days the nerves of the transplanted heart are completely regenerated and the connection of these nerves with the organism of the recipient is established. At about this time, the work of the heart also changes considerably: the heart begins to respond to pain irritations by an acceleration of its beat. Furthermore, the arterial pressure increases to a normal value. The frogs on which the experiments have been carried out survive for more than 12 months. In the spring they croak cheerfully and spawn.

As far as vertebrates are concerned, we have successfully carried out the transplantation of whole organs from one animal to another for the first time. The reports on the transplantations of glands of internal secretion which had been made hitherto were not supported by histological data. These data are absolutely necessary, however. A temporary restoration of the disturbed hormonal function in the organism cannot be regarded as going beyond mere hormone therapy.

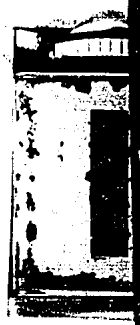
It is true that transplantations of kidneys and legs to dogs have yielded good results recently. These experiments were carried out by Soviet scientists (Lapchinskiy, Shpuga, Vishnevskiy, Mazayev, and Chepov). In these experiments, the method of preliminary storage at low temperatures and in artificial nutrient media of the organs being transplanted was also used.

Our research on the transplantation of the heart to frogs is of significance for the solution of the problem in question as far as warm-blooded animals and human beings are concerned. The work on the transplantation of hearts to warm-blooded animals, which has been studied since 1933, is carried out with consideration for the results obtained in work on cold-blooded animals. We successfully transplant second hearts to dogs and cats into the neck, into the abdominal cavity, or into the chest. In conducting these experiments, we investigate the effects of sleep therapy and of artificial nutrient media in combination with hypothermia.

A method of visual observation of the coronary circulation in warm blooded animals has been developed and applied in our laboratory since 1951. This method is very important for the investigation of various forms of coronary insufficency arising after the transplantation of the heart or in various experimentally induced diseases.

At present we have completely mastered the method. To apply it, we developed a special type of cannula made of transparent plastic and equipped with a hermetic closure. This cannula heals into the chest of the dog in the region of the heart. The operation resulting in the healing-in of the cannula is carried out in three stages, after preliminary removal of the left lung. A cannula of this type makes it possible to observe the coronary circulation of the dog not only with the naked eye but also by means of a microscope, with the result that the circulation is observed not only in large blood vessels, but also within the capillary network of the heart.

Direct access to the heart muscle is possible through the cannula. This means that it is possible to affect experimentally both the heart muscle and the blood vessels of the heart. By tying up the coronary vessels or introducing semiliquid paraffin wax into them, one may easily bring about partial interference with the coronary circulation, so that a miocardial infarction results.



With the aid of our method, it is possible to study all stages of the development of this dangerous heart disease and clarify the therapeutic effectiveness of various drugs. This is not only of theoretical, but also of practical importance.

By means of the cannula grown into the pericardium, one may also investigate the process of the healing of the heart muscle subsequently to the experimental infliction of wounds. It is possible to stitch the wounded heart and investigate the effect of various drugs, for instance vitamin C, on the process of scar formation on the heart muscle.

We are able to study the reaction of both muscular and nerve elements of the heart to the introduction into the heart muscle of foreign bodies such as iron, lead, platinum, glass, etc., and to observe the course of various processes resulting from injuries to the heart as well as methods of treating these injuries.

Simultaneously with the investigation of morphological changes in the heart after experimentally induced diseases, one may observe changes in the volume of the heart, i.e., measure the heart's power of contraction.

To carry out these measurements, we designed a special apparatus with the aid of which one can easily record on a kymograph the contractile power of the heart and its volume at any position of the body of the animal.

We also used successfully cannulas of transparent plastic for observing the blood circulation in the organs of the abdominal cavity. In order to carry out these observations, we let the cannula grow in above the liver, the kidney, or the intestine. With the use of this method extensive possibilities are opened up of studying experimentally the blood circulation and the course of various pathological processes in organs of the abdominal cavity. These experiments were carried out on dogs.

We also study in our laboratory the action of various toxic chemical substances on the functioning of transplanted organs. We have worked for more than 10 years on problems of this type, which have a direct bearing on the transplantation of organs and the primary mechanism of the action of poisons on the organism.

We have set ourselves the task of investigating the action of alcohol and of nicotine on the blood vessels of the brain. We wanted to investigate how the reactivity of the blood vessels of the brain changes under the action of these substances, or in other words, to find out to what extent the vasodilative or vasoconstrictive effects produced by various substances after the animals have been subjected to chronic poisoning with alcohol or nicotine deviate from normal reactions caused by these substances. For this purpose we developed the method of transplanting a second head onto the neck of a dog.

We endeavor to create conditions for the surviving second head which correspond as closely as possible to conditions of normal nutrition. Furthermore, we eliminate completely all influences affecting the blood vessels which arise from internal organs that are also poisoned with the substances in question. In order to eliminate these factors, we found it expedient to implant a second head.

Experiments on the transplantation of isolated dogs' heads and of the heads of other animals were already carried out in the 19th Century. Experiments of this type have been conducted by the Russian scientists A.A. Kulyabko and S.I. Chechulin. S.S. Bryukhonenko designed for this purpose a very complicated appliance, called the autojector, which replaces the heart and requires the addition of an anticoagulant to the blood circulated by it.

In our experiments we try to create for the surviving [transplanted] dogs head conditions which are as close as possible to normal. We developed a new method of resuscitating the head of the dog in connection with its transplantation onto the neck of another dog.

Essentially our method amounts to establishing a preliminary anastomosis between the carotid arteries and jugular veins of the two animals. The order in which the anastomosis is carried out enables the blood emerging from the central endings of the arteries of the donor to flow into the peripheral ends of the carotid arteries of the recipient, i.e., of the second [transplanted] head, while the veins of the transplanted head are connected with the central ends of the veins of the dog which supplies the blood circulated in the second head.

After the blood circulation in the second head has been restored by letting the blood from the other animal flow into it, the head to be transplanted is cut off the body. After 5-6 minutes, the head that has been cut off begins to show signs of life: it opens its mouth, licks itself, blinks its eyes, and looks around attentively. When called, the head turns its eyes in the direction from which it has been called, raises its ears, and attempts to bark. It reacts violently to irritations of the ear by means of sound, of the nose with smoke, and of the tongue with bitter substances, i.e., evinces all signs of life which are susceptible of observation.

After this preliminary preparation, when the head has been brought to a calm and relatively normal state, we start our experiments. By introducing into the blood vessels of the second head various vasoconstrictive or vasodilative substances, we are able to determine the difference between the reactions of the blood vessels of a head poisoned with alcohol or nicotine and the reactions of the vessels in a head not poisoned with these substances.

In 1954, a communication was published by V.P. Demikhov, who used our method of grafting a second head onto a dog.

The experiments that have been described may yield new data on the degree and rate of affliction of cerebral blood vessels with poisons and also on the effectiveness of the action of drugs whenever spasms or sclerosis of the blood vessels of the brain have been brought about by alcohol or nicotine.

All the experimental work done by us has the single purpose of studying and alleviating the severe ailments resulting from premature deterioration of the heart and of the blood vessels of the brain.

- E N D -